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Acute Hepatitis C Viral Infection During Pregnancy: Failure of Mother to Infant Transmission

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A pregnant woman developed an acute hepatitis C virus (HCV) type 3a infection during the second trimester of pregnancy. The clinical virological features are presented, including HCV RNA quantification of maternal serum samples collected during pregnancy. These findings are discussed in light of the child's remaining uninfected after 5 years of follow-up. ***J. Med. Virol. 52:161–163, 1997.*** © 1997 Wiley-Liss, Inc.

KEY WORDS: acute HCV infection; pregnancy; HCV RNA quantification; type 3a; transmission failure

INTRODUCTION

There are conflicting reports regarding the extent of mother-to-infant transmission of hepatitis C virus (HCV) infection [Reesink et al., 1990; Inoue et al., 1991; Thaler et al., 1991; Lam et al., 1993; Wejstål et al., 1992; Reinus et al., 1992]. Recent studies have indicated that women coinfected with HIV have a greater risk of transmitting HCV vertically, possibly due to the increased HCV load associated with the presence of immunosuppression [Zanetti et al., 1995]. This suggestion is supported by the findings of a prospective study of pregnant chronic HCV carriers in whom the risk of transmission was correlated with the maternal serum HCV RNA titre [Ohto et al., 1994].

These and other reports of vertical transmission have focused on chronic HCV carriers. However, the risk of transmission related to acute HCV infection in pregnancy is unknown. We report on the clinical, serological, and molecular virological findings in a woman who developed an acute HCV infection during pregnancy and whose child was not infected.

CASE REPORT

A 23-year-old woman visited Pakistan with her family, when she was 12 weeks pregnant, between April and July 1991. Her pregnancy progressed uneventfully until October, when, at 29 weeks, she was icteric, with no other findings of note on examination. Ultrasound of the liver and common bile duct was normal, haemoglobin was 10.5 g/dl, urinalysis revealed bilirubinuria, and the liver function tests were abnormal with alanine aminotransferase 123 IU, alkaline phosphatase 186 IU, and bilirubin 97 μmol/l. Hepatitis A IgM, hepatitis B surface antigen and hepatitis C antibody (Ortho, HCV ELISA Test System, second generation, Raritan, NJ) were not detected. There was evidence of past cytomegalovirus and Epstein-Barr virus infection, and hepatitis E was considered as part of the differential diagnosis.

The baby had a normal full-term delivery on November 14, 1991. A further maternal serum specimen was tested for HCV antibody and was reactive with a test/cut-off value of 1.9 which had risen to 2.6 within 4 days. A C33 band was seen on the supplementary recombinant immunoblot assay RIBA-2 (Chiron RIBA HCV Test System, second generation, Raritan, NJ). The presence of HCV antibody was confirmed by January 1992 (Table I). A careful history was taken and no risk factors for acquiring hepatitis C were ascertained.

HCV antibody was not detected in serum collected from the baby at birth. The lack of passively acquired maternal antibody was thought to be because HCV seroconversion occurred at a time between October 10 and November 18. It was therefore likely that the mother was highly infectious at the time of delivery.

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TABLE I. HCV Serology, HCV RNA Detection and Quantification, and Liver Function Test Results

Subject	Date	Anti-HCV ELISA NOD[a]	RIBA-2	Qualitative HCV RNA	Quantitative HCV RNA copies/ml	ALT IU	Bilirubin μmol/l
Mother	07/30/91	Negative	ND[b]	Positive	2×10^6	ND	ND
	10/10/91	Negative	ND	Positive	4×10^7	123	97
	11/18/91	1.9	ND	Positive	$>10^8$	ND	ND
	11/22/91	2.6	c33 only	Positive	ND	ND	ND
	01/20/92	3.1	c33, c100 tr, c22 tr	ND	ND	775	19
	05/15/92	ND	ND	ND	ND	252	ND
	09/23/92	ND	ND	ND	ND	66	6
	01/10/95	ND	ND	ND	ND	69	6
	10/10/95	ND	ND	ND	ND	56	6
Baby[c]	01/16/92	Negative	ND	Negative	ND	ND	ND
	02/26/92	Negative	ND	Negative	ND	ND	ND
	10/10/92	ND	ND	Negative	ND	ND	ND
	12/95	Negative	ND	Negative	ND	ND	ND
Father	01/16/92	Negative	ND	Negative	ND	48	6
Daughter 1	01/16/92	Negative	ND	ND	ND	ND	ND
Daughter 2	01/16/92	Negative	ND	ND	ND	ND	ND

[a]Normalised optical density = test value/test cut-off.
[b]Not done.
[c]Date of birth 14/11/91 tr = trace.

HCV RNA was detected in maternal serum samples collected on July 30, October 10, and November 18, 1991, by an in-house nested polymerase chain reaction (PCR) assay using primers based on the highly conserved 5′ non-coding region [Garson et al., 1990]. The HCV infection was type 3a [Davidson et al., 1995]. The mother decided to breast-feed, and HCV RNA was not detected in a sample of breast milk. Aliquots of maternal sera stored at –20°C were tested retrospectively by a quantitative HCV RNA method [Whitby and Garson, 1995]. By the time of delivery the level of HCV viraemia had risen by at least 2 $\log_{10}$ (Table I).

A liver biopsy in April 1993 was consistent with chronic hepatitis. Interferon alpha at 3MU 3 times per week was given in January 1995 but was discontinued after 3 months due to a lack of response.

HCV RNA was not detected in serum samples collected from the baby over 10 months, and neither HCV antibody nor HCV RNA was detected when the child was 4 years of age.

HCV antibody was not detected in serum samples collected from the father and the two other children in January 1992 or in serum samples from all three children in 1995.

DISCUSSION

It is difficult to compare directly the level of viraemia with that in another report which demonstrated a reduced risk of vertical transmission of HCV where less than 10^6 HCV RNA copies were detected per ml of maternal sera [Ohto et al., 1994] because different methods of HCV RNA quantification have been used. However, it is somewhat surprising that the baby remained uninfected after the mother had developed an acute HCV infection during pregnancy, with $>10^8$ HCV RNA copies/ml around the time of delivery. The very high titre was consistent with the recognised peak titre in the acute phase of an HCV infection.

HCV RNA was not detected in the breast milk, which corresponded with findings reported by others [Manzini et al., 1995; Hsu et al., 1991; Kurauchi et al., 1993]. It is relevant to note that the assay volume was significantly less than an average feed and that the possibility of a sampling error should be considered. HCV RNA detection in such specimens could be improved by incorporating a concentration and RNA extraction step before genome amplification. However, transmission did not occur even though the baby was breast-fed.

One might speculate that in addition to the level of viraemia, the HCV genotype may influence the risk of transmission. Although materno-fetal transmission did not occur after this acute type 3a infection, a prospective study reported 6 children with HCV infection born to mothers with HCV antibody, some of whom had HIV coinfection. Four children had HCV genotype 3a infections. Three were born to mothers with HIV coinfection; the other woman had HCV-related chronic active hepatitis [Zuccotti et al., 1995].

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